

encountered in the case reported here because the twins were of different sexes. However, when the twins are of the same sex chromosome polymorphism studies should be carried out, even though low banding resolution seems to be a characteristic of chorionic villi chromosomes. Whenever villi specimens are taken for metabolic or DNA studies⁴⁻⁶ fetal karyotyping should help to establish reliable results from each twin.

In conclusion, the discovery of twins at the time of chorionic villi sampling creates concern regarding the ability to diagnose each twin, but this should not be a contraindication to the use of the aspiration technique. By taking samples at the insertion site of the umbilical cord, good reliability in sampling the two different chorionic tissues is attained. Chromosome polymorphism study of the karyotype of the parents and fetus is indicated when the same sex chromosome constitution is present in all the aspirated specimens analysed.

Fetal karyotyping proves to be a very advantageous preliminary approach when chorionic villi are used for metabolic and DNA studies. Sufficient chorionic tissue should always be taken to perform chromosome analysis regardless of the indication for the fetal diagnosis. A very small amount of villi is required for fetal karyotyping using the direct method. If it proves impossible to

obtain samples from both twins, or if one of the twins is shown to be chromosomally abnormal, any decisions on the outcome of the pregnancy should be deferred until amniocentesis or fetoscopy have been performed.

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Cat eye syndrome owing to tetrasomy 22pter→q11

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SUMMARY A case of tetrasomy 22pter→q11 with ocular hypertelorism, downward slanting palpebral fissures, total anomalous pulmonary venous return, and anal atresia is described. The phenotypic variability of the cat eye syndrome is emphasised along with the need for categorisation of these patients according to well characterised cytogenetic findings.

Since the original description of four patients with a small extra chromosome,¹ the delineation of the cat eye syndrome² has been hindered by both phenotypic and cytogenetic variability. Certain component defects of the cat eye syndrome, such as

the ocular colobomata, preauricular tags, anal atresia, cardiac anomalies, and renal anomalies, occur in a variety of disorders including the VATER and CHARGE associations. Schinzel *et al*³ provide convincing evidence that the extra small chromosome associated with the cat eye phenotype represents trisomy or tetrasomy of 22pter→q11 rather than the phenotypically different trisomy 22,⁴ translocation 11;22,⁵ or tetrasomy 15pter→q11-13.⁶ Syndromes caused by these distinct cytogenetic entities can now be defined and separated from non-chromosomal causes of the cat eye phenotype.⁷

Case report

The patient was the 3 kg (40th centile), 52 cm (60th centile) male product of an uncomplicated 37-week gestation. The mother, aged 27, and the father, aged

30, had had no previous pregnancies, were unrelated, and had no family history of birth defects or mental retardation. After a spontaneous vaginal delivery, the child was referred for evaluation of imperforate anus and other anomalies including a single umbilical artery. Physical examination disclosed a mildly abnormal facies (fig 1) with hypertelorism. The interpupillary distance was 4.5 cm (90th centile). There was an antimongoloid slant to the eyes, depressed lower eyelids, and micrognathia. The right external auditory meatus was atretic and there were bilateral preauricular skin tags. There were no colobomata of the irides or fundi. There was a continuous cardiac murmur which was caused by total anomalous pulmonary venous return to the innominate vein with an atrial septal defect. The genitalia were normal above a smooth perineum and a blind anal dimple. A high imperforate anus with a rectovesical fistula was documented at surgery.

After sigmoid loop colostomy at the age of 2 months, sacroperineal pullthrough at the age of 9 months, and total cardiac repair at the age of 14 months, the patient's growth retardation resulting from hypoxaemia, pulmonary hypertension, and chronic constipation improved. At 27 months his height was 89 cm (40th centile) and his weight was 11.7 kg (20th centile) with a normal growth velocity. A follow-up cardiac catheterisation revealed no residual shunts. A mild right conductive hearing loss was documented. Intellectual development is delayed, but progress since surgery has improved to the point where the patient has normal motor skills.

CYTOGENETIC RESULTS

A Giemsa-trypsin banded karyotype using standard methods demonstrated an extra bisatellited chromosome fragment in 25 out of 25 cells (fig 2a). The presence of NOR material at both ends was demonstrated (fig 2b) by silver staining⁸ and satellite association with other acrocentric chromosomes.

The ends of the fragment were negative for C banding or DAPI staining.⁶ The karyotype is consistent with a description 47,XY,+iso (22pter→q11).

Discussion

The report of Schinzel *et al*³ was the first to separate cases of the cat eye syndrome with presumed or documented tetrasomy 22pter→q11. We add another case documented by silver staining and strongly support their approach in delineating specific phenotypic-cytogenetic correlations in the cat eye syndrome. Identification of the bisatellited fragment is partly based on phenotypic resemblance to patients with trisomy 22pter→q11 identified by familial translocations.³ Tetrasomy 15p was clearly ruled out by DAPI staining and the phenotypic differences summarised by Van Dyke *et al*.⁶ The small extra fragment resulting from 11q;22p translocation⁵ can also be distinguished by phenotypic correlation and silver staining. Robertsonian translocation between chromosomes 22 and 13 was suggested by Petit *et al*⁹ as the cause for the marker chromosome in their case since there was asymmetry both for length and silver staining. Guanti⁷ also suggested involvement of chromosome 13 based



FIG 1 Front and lateral views of the proband.

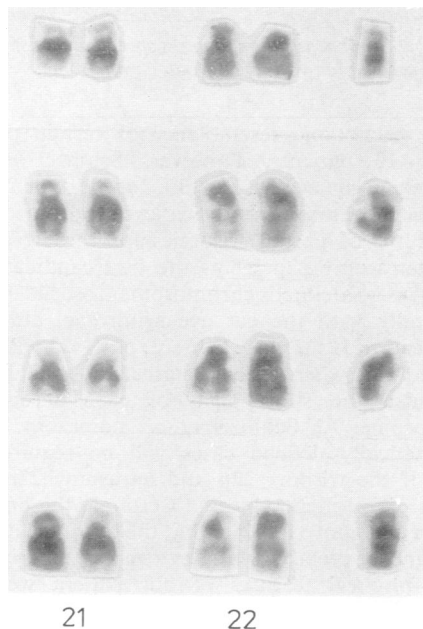


FIG 2 (a) Giemsa-trypsin banded partial karyotype of the proband showing the symmetrical bisatellited extra chromosome.



FIG 2 (b) Silver stained metaphase spread demonstrating the symmetrically NOR positive extra chromosome in satellite association with a D group chromosome.

on the phenotypic resemblance of certain partial trisomy 13 patients. However, Schinzel *et al*³ effectively argue against iso 13p, 14p, 15p, or 21p as the extra chromosome in the cat eye syndrome based on features of partial trisomies for these regions. Thus, tetrasomy 22p seems the best candidate for the extra bisatellited chromosome associated unequivocally with the cat eye syndrome, although translocation 13;22, 14;22, 15;22, or 21;22 will only be ruled out when specific stains are available to distinguish the short arms of each acrocentric chromosome. As Schinzel *et al*³ point out, more cytogenetically defined cases will be required to decide if the trisomy 22p and tetrasomy 22p syndromes differ phenotypically. Certainly the findings summarised above indicate that the term 'the cat eye syndrome' be prefaced with a cytogenetic description.

The physical features of our patient were of interest since the depression of the lower eyelid may represent minimal expression of a coloboma. This patient emphasises that the colobomata are not essential features of trisomy or tetrasomy 22p³ and that suspicion must be high to detect a chromosome

abnormality in these relatively normal looking patients. Also of interest is the total anomalous pulmonary venous return which is becoming identified as a characteristic heart defect in the iso 22p cat eye syndrome. Adding our case to the series of Schinzel *et al*,³ five of 11 patients with tetrasomy 22p had heart defects, of which four were total anomalous pulmonary venous return. Early recognition and correction of this anomaly is important because of the associated pulmonary hypertension.

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Triploidy with cyclopia and identical HLA alleles in the parents

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SUMMARY A 22-week pregnancy was terminated after discovery of serious echographic abnormalities. Fetal examination showed cyclopia, sacral meningocele, and syndactyly. The karyotype was 69,XXX. The parents had identical HLA alleles A1, A2, and Bw21. The mechanism of the triploidy was determined by chromosome marker analysis to be digyny. The association of triploidy with holoprosencephaly and the parents' identical immunological status are discussed.

Triploidy is a common chromosomal abnormality, occurring in about 2% of human conceptuses. As a general rule these abnormal embryos are spontaneously aborted early in gestation.¹ The present article reports a case of triploidy which is unusual for the following reasons: the survival of the fetus to 22 weeks; the rare association of triploidy with holoprosencephaly; and the discovery of identical HLA -A and -B alleles in the parents.

Case report

A 22-week fetus was aborted abdominally. The 23-year-old G2, P1 mother had had an apparently normal stillborn fetus 2 years earlier. This was followed by treatment for hyperthyroidism. The mother and her healthy 29-year-old husband were not consanguineous and the family history was unremarkable.

The second pregnancy proceeded normally until

the 21st week when uterine sonography revealed an increased cranial diameter for gestational age and absence of median echo as well as a caudal mass. Elective abortion was performed in the 22nd week.

Examination of the female fetus confirmed the echographic diagnosis of sacral meningocele with hydrocephalus and revealed the presence of cyclopia (fig 1). The head had a single diamond-shaped orbit, surrounded by four rudimentary eyelids located in the middle of the face and containing a single eyeball. A fleshy supraorbital proboscis was present with a terminal dimple. The philtrum was absent and the mouth was small. There was complete syndactyly between fingers 3 and 4 of both hands.



FIG 1 The fetus.